



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

a major reservoir of group A streptococcus: up to 15–25% of asymptomatic school-aged children are colonised in their throat.⁴ Children can transmit group A streptococcus to their pregnant mothers or to other contacts. Screening for children has not been found to be feasible or desirable.⁴ However, screening of health-care givers who have cared for patients admitted with serious group A streptococcal infection has been recommended⁴ to limit the spread of infection.

Group A streptococcal disease in pregnant women and young children is serious. Knowledge of the different clinical features of invasive group A streptococcal infection could lead to earlier recognition and treatment of infection, data on invasive disease would improve, and more correct estimates of disease would be available. Increased knowledge might improve the evaluation of treatment and the development of preventive strategies such as screening or vaccine development.

I declare no competing interests.

Rikke Bek Helmiq

rikke.bek.helmiq@dadlnet.dk

Aarhus University Hospital Skejby, Højbjerg, 8270, Denmark

- 1 Sherwood E, Vergnano S, Kakuchi I, et al. Invasive group A streptococcal disease in pregnant women and young children: a systematic review and meta-analysis. *Lancet Infect Dis* 2022; published online April 4. [https://doi.org/10.1016/S1473-3099\(21\)00672-1](https://doi.org/10.1016/S1473-3099(21)00672-1).
- 2 Gustafson LW, Blaakær J, Helmiq RB. Group A streptococci infection. A systematic clinical review exemplified by cases from an obstetric department. *Eur J Obstet Gynecol Reprod Biol* 2017; **215**: 33–40.
- 3 Tarvade S, Lane AS. Ante-partum necrotising myometritis due to streptococcal toxic shock. *J Intensive Care Soc* 2015; **16**: 172–78.
- 4 Donders G, Greenhouse P, Donders F, Engel U, Paavonen J, Mendling W. Genital tract GAS infection ISIDOG guidelines. *J Clin Med* 2021; **10**: 2043.
- 5 Shinar S, Fouks Y, Amit S, et al. Clinical characteristics of and preventative strategies for peripartum group A streptococcal infections. *Obstet Gynecol* 2016; **127**: 227–32.
- 6 Udagawa H, Oshio Y, Shimizu Y. Serious group A streptococcal infection around delivery. *Obstet Gynecol* 1999; **94**: 153–57.
- 7 Arai T, Takai Y, Samejima K, Matsunaga S, Ono Y, Seki H. How could we suspect life-threatening perinatal group A streptococcal infection? *J Obstet Gynaecol Res* 2020; **46**: 2573–81.
- 8 Sosa MEB. Group A streptococcal infection in pregnancy and the puerperium. *J Perinat Neonatal Nurs* 2016; **30**: 124–30.
- 9 Harrington DH, Lenahan CM, Sanders RM. A practitioner's guide to necrotizing fasciitis. *Nurse Pract* 2015; **40**: 48–54.

Monkeypox outbreaks outside endemic regions: scientific and social priorities



As the world recovers from the shock of the COVID-19 pandemic and reflects on lessons learnt from failure of global public health systems to contain the global outbreak of SARS-CoV-2,¹ new infectious disease threats, caused by movement of people globally, remain omnipresent, and repeated calls² for more proactive action go unheeded. This is aptly shown by the unprecedented and unexpected outbreaks of human monkeypox cases and clusters since May 7, 2022, across Europe, the Americas, and Australia,³ which yet again, have taken global public authorities by surprise.

In the ongoing outbreak, the first monkeypox case reported by the UK Health Security Agency on May 7, had travel links to Nigeria.⁴ On May 14, two more cases were identified in the UK, both lived in the same household but had no travel history to Africa and no contact with the case reported on May 7. Additional monkeypox cases have continuously been reported to WHO from 12 member states across three WHO regions. As of May 21, 2022, there have been 92 laboratory-confirmed cases and 28 suspected monkeypox cases reported to WHO from the UK, the USA, Canada, France,

Germany, Belgium, Spain, Portugal, Italy, Sweden, and Australia.³ Detection of more cases is anticipated. The epidemiological links between these cases remain to be defined. Fortunately, there have been no deaths reported to date. However, there are several unusual, atypical, and perplexing aspects of these outbreaks that are of major scientific, public health, and social concern.

First, the number of monkeypox cases detected in this outbreak 2 weeks since first case detection³ in the UK alone has, by far, surpassed the total number of cases detected in the UK⁵ and outside monkeypox-endemic Africa zones² since the first discovery of monkeypox in 1970 as a human pathogen. The scientific, environmental, and social reasons for this phenomenal increase remain an enigma and require urgent delineation through a unified, universal One Health (human, environmental, and animal) approach.²

Second, it is very unusual and worrying that ongoing epidemiological investigations to date have revealed no substantial travel links of the cases to monkeypox-endemic areas in Africa.^{2,3} This could indicate that the monkeypox virus might already have been spreading



Published Online
May 27, 2022
[https://doi.org/10.1016/S1473-3099\(22\)00354-1](https://doi.org/10.1016/S1473-3099(22)00354-1)

undetected in Europe for a while, with human-to-human transmission occurring due to close physical contact with infected asymptomatic or symptomatic people.

Third, whether these events are due to change in monkeypox virus transmission properties or increased virulence remains unknown. Compared with RNA viruses, the monkeypox virus is a large DNA virus, which makes itself more stable and efficient than RNA viruses at detecting and repairing mutations. Thus, it is unlikely that the virus has evolved to increase human transmission. Preliminary genomic sequence data indicate a relationship with monkeypox clades circulating in west Africa, which cause milder disease and have a lower death rate than clades in central Africa.³

Fourth, most monkeypox cases have been detected in men who have sex with men³ and some cases in Europe occurred in men who have sex with men and bisexual men who travelled to recent festivals. Whether monkeypox is sexually transmitted requires further careful study in all geographical settings. Clusters of viral infections can occur in any group in close contact at mass gathering events.⁶ The intense public and social media coverage regarding the spread of monkeypox in these contexts has generated hype in its various forms through use of language, conversation, and content, indirectly or directly negatively generating homophobic and racist stereotypes that exacerbate stigma.⁷ This is prejudicial, unfair, stigmatising, and unacceptable.^{7,8} Lessons from the HIV and AIDS response showed that stigma and blame undermines outbreak response,⁸ highlighting the universal need for building human-rights-based, non-stigmatising outbreak responses and community-led epidemic prevention programmes.

Fifth, the monkeypox outbreaks expose major gaps in understanding the dynamics of viral transmission and continuously evolving epidemiological characteristics of the disease,^{2,5,9} and a more coordinated approach to epidemic preparedness is long overdue.¹² Most monkeypox cases in the current outbreak are in men aged 20–50 years. Smallpox vaccination was discontinued worldwide in the 1980s and cases of monkeypox in Africa were comparatively small before this.^{2,9,10} This increase in numbers in this age group might reflect the loss of cross-protective immunity to monkeypox from not receiving the smallpox vaccination.^{2,10} The antiviral tecovirimat for treatment of

seriously ill monkeypox cases, and the third-generation smallpox vaccine Imvanex (Bavarian Nordic, Hellerup, Denmark) for use as prophylaxis in all close and high-risk case contacts, together with specific guidelines for their use, need to be made available urgently universally at affordable cost.

Sixth, the appearance and rapid spread of monkeypox in Europe has generated intense scientific, political, and media activity. The rapid pace of developments, increasing case-detection rates, and accumulating real-time evolving data from global public health authorities have fuelled public anxieties. Two-way communication on monkeypox-related risks and engagement of affected communities on prevention, detection, and care becomes important for preventing further spread of monkeypox.

Seventh, in nature, the monkeypox virus transmits to humans from either rodents or from infected humans. Hundreds of cases of human monkeypox are detected in west and central Africa annually. The few cases seen outside Africa have all been associated with travel to Africa or contact with imported infected rodents.^{2,5,9} The role of rodents in the UK monkeypox cases with history of travel to Africa^{4,5,9} might reflect the current wave of human monkeypox infections occurring in Nigeria consequential to increased exposures to rodents during the COVID-19 lockdown periods. These secondary epidemiological cycles with human-to-human spread might be affecting international travellers. Further study on rodent dynamics and monkeypox cases inside and outside endemic regions aligned to viral genomics is required to detect possible drivers for the current monkeypox epidemic.

Priority for the current monkeypox outbreak should be on stopping further spread and protecting frontline health-care workers, and those most at risk globally. The unprecedented manifold increase in monkeypox cases seen in the past 3 weeks outside Africa yet again highlights that developing effective capacity at source is crucial for effective global public health preparedness and surveillance for zoonotic threats to global health security.¹² Rapid garnering of financial and political support for this is required to fuel reassurance, rather than fear and stigmatisation.

AZ, NH, DA, FN, and RK are members of the Pan-African Network for Rapid Research, Response, Relief and Preparedness for Infectious Diseases Epidemics funded by the European and Developing Countries Clinical Trials Partnership, which is supported by Horizon 2020, the EU's Framework Programme for

Research and Innovation. AZ holds a UK National Institute of Health Research Senior Investigator Award and is a Mahathir Science Prize and Pascoal Mocumbi Prize laureate. All authors have an interest in epidemic infections.

*Alimuddin Zumla, Sofia R Valdoeiros, Najmul Haider, Danny Asogun, Francine Ntoumi, Eskild Petersen, Richard Kock

a.zumla@ucl.ac.uk

Department of Infection, Division of Infection and Immunity, Centre for Clinical Microbiology, University College London, London, UK (AZ); NIHR Biomedical Research Centre, University College London Hospitals NHS Foundation Trust, London NW1 OPE, UK (AZ); Infectious Diseases Department, Centro Hospitalar Universitário de São João, Porto, Portugal (SRV); The Royal Veterinary College, North Mymms, Hatfield, Hertfordshire, UK (NH, RK); Irrua Specialized Teaching Hospital, Irrua, Nigeria (DA); Congolese Foundation for Medical Research, Brazzaville, Republic of the Congo (FN); Institute for Clinical Medicine, Aarhus University, Aarhus, Denmark (EP)

- 1 Ntoumi F, Zumla A. Advancing accurate metrics for future pandemic preparedness. *Lancet* 2022; **399**: 1443–45.
- 2 Petersen E, Abubakar I, Ihekweazu C, et al. Monkeypox—enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era. *Int J Infect Dis* 2019; **78**: 78–84.
- 3 WHO. Multi-country monkeypox outbreak in non-endemic countries. May 21, 2022. <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385> (accessed May 22, 2022).
- 4 UK Health Security Agency. Monkeypox cases confirmed in England—latest updates. May 14, 2022. <https://www.gov.uk/government/news/monkeypox-cases-confirmed-in-england-latest-updates> (accessed May 20, 2022).
- 5 Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis* 2022; published online May 24. [https://doi.org/10.1016/S1473-3099\(22\)00228-6](https://doi.org/10.1016/S1473-3099(22)00228-6).
- 6 Memish ZA, Steffen R, White P, et al. Mass gatherings medicine: public health issues arising from mass gathering religious and sporting events. *Lancet* 2019; **393**: 2073–84.
- 7 UNAIDS. UNAIDS warns that stigmatizing language on monkeypox jeopardises public health. May 22, 2022. https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2022/may/20220522_PR_MONKEYPOX (accessed May 22, 2022).
- 8 Fischer LS, Mansergh G, Lynch J, Santibanez S. Addressing disease-related stigma during infectious disease outbreaks. *Disaster Med Public Health Prep* 2019; **13**: 989–94.
- 9 Petersen E, Kantele A, Koopmans M, et al. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. *Infect Dis Clin North Am* 2019; **33**: 1027–43.
- 10 Simpson K, Heymann D, Brown CS, et al. Human monkeypox—after 40 years, an unintended consequence of smallpox eradication. *Vaccine* 2020; **38**: 5077–81.

COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England



The omicron (B.1.1.529) variant, first detected in the UK on Nov 27, 2021, rapidly became the dominant strain, due in part to reduced vaccine effectiveness.¹ An increase in sequenced cases of the omicron sub-lineage BA.2 was observed in the week beginning on Jan 3, 2022.² BA.2 has a growth advantage over BA.1^{3,4} and has become the dominant strain in the UK at the time of writing. Neutralisation assays using monoclonal antibodies have suggested a small antigenic difference between BA.1 and BA.2, although sera from individuals with booster vaccinations neutralise both variants similarly.³

The UK COVID-19 vaccination programme has been in place since Dec 8, 2020, with primary courses of two doses of either BNT162b2 (Comirnaty, Pfizer–BioNTech), ChAdOx1-S (Vaxzevria, Oxford/AstraZeneca), or mRNA-1273 (Spikevax, Moderna). Booster vaccination with either BNT162b2 or a half dose (50 µg) of mRNA-1273 was introduced on Sept 14, 2021, to adults older than 50 years and those in risk groups, and on Nov 29, 2021, to all adults.

In this Comment, we estimate vaccine effectiveness against symptomatic disease and hospitalisation with BA.1 and BA.2 after one or two doses of BNT162b2,

ChAdOx1-S, or mRNA-1273, and after booster doses of BNT162b2 or mRNA-1273 during a period of co-circulation. We used a test-negative case-control study design.^{5–8} Our analysis included all vaccines used in the UK. Vaccination status was included as an independent variable and effectiveness defined as 1 minus the odds of vaccination in cases, divided by the odds of vaccination in controls (appendix pp 1–3).

Between Jan 17 and March 31, 2022, there were 1127517 eligible tests from symptomatic individuals, of which 265 820 were positive for BA.1, 246 069 were positive for BA.2, and 615 628 were negative (controls). The hospitalisation analysis included 15043 eligible tests, of which 1662 were positive for BA.1, 623 were positive for BA.2, and 12758 were controls (appendix pp 4–7).

There was no evidence of reduced vaccine effectiveness against symptomatic disease with BA.2 compared with BA.1 (figure; appendix p 9). 25 weeks or more after two doses, vaccine effectiveness was 14.8% (95% CI 12.9–16.7 against BA.1 and 27.8% (25.9–29.7) against BA.2. Booster immunisation increased protection after a week to 70.6% (68.9–72.2)

Published Online
May 24, 2022
[https://doi.org/10.1016/S1473-3099\(22\)00309-7](https://doi.org/10.1016/S1473-3099(22)00309-7)

See Online for appendix